International
BIOLOGICAL THREAT REDUCTION

The Biological Weapons Threat: A US Perspective

Sandia National Laboratories

Laboratory Biosecurity and Biosafety Workshop

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NNSA National Nuclear Security Administration

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State Biological Weapons History

- **State BW Use**
  - **World War I**
    - **Germany, France**
  - **World War II**
    - **Japan, USSR**
  - **Other incidents**
    - **Bulgarian assassination, South African BW program activities**
- **General Pattern of State BW use**
  - **State BW programs have conducted research on a wide array of agents, including those that cause high fatality diseases**
  - **Wide dissemination capabilities**
  - **Potential to cause a high consequence BW event**
  - **Willingness to use BW during wartime conditions**
  - **Intent and effect of BW use has been tactical, not strategic**

Bioterrorism in the US: 1984

- September 17, 1984 – First reports of gastroenteritis from recent patrons of restaurants in The Dalles, Oregon
- Laboratory tests confirm *Salmonella typhimurim*
- Outbreak:
  - 751 cases of salmonella poisoning but
  - No fatalities
- CDC investigation concludes that outbreak resulted from food handlers' inadequate hygiene
- September 16, 1985 – rift between cult member and leader reveals incident was not a natural outbreak

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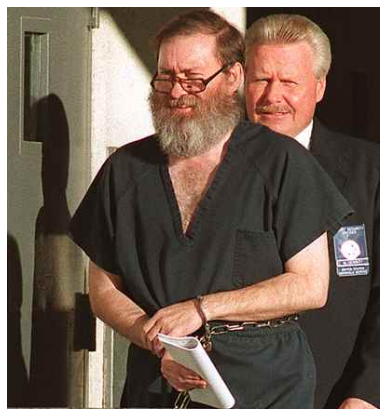
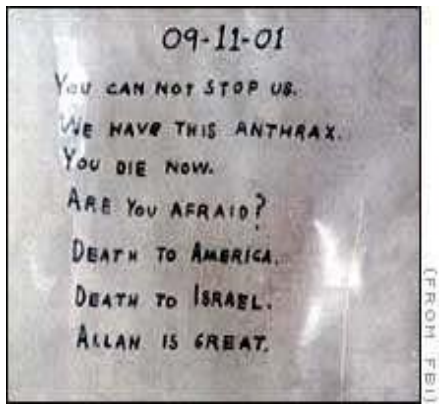
Bioterrorism in the US: 1995

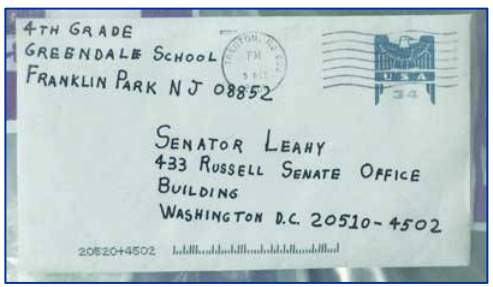
- May 1995 – Larry Wayne Harris ordered 3 vials of *Yersina pestis* from the American Type Culture Collection
- Arrested for obtaining the bacteria through falsified documents
  - Possession not a crime in 1995
- Led to the original Select Agent List – only regulated transfers
  - Anti-terrorism and Effective Death Penalty Act of 1996

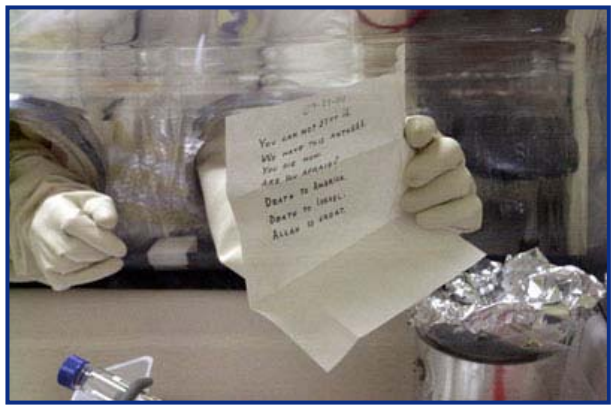


Bioterrorism in the US: 2001

- **Fall 2001 anthrax attacks**
  - **Highly refined: 4-7 letters contaminated over 60 different sites**
    - **Sent to news outlets and US Congress**
  - **Highly virulent: Kills 5, wounds 21**
  - **Perpetrator(s) still unknown**







Non-State Biological Weapons History

- **Major incidents of bioterrorism**
  - **2001 Anthrax attacks in the US**
  - **1990s Aum Shinrikyo attempts**
  - **1984 Rajneeshee religious cult attacks**

- **Continued perpetration of biocrimes of minor consequence**

- **General pattern of bioterrorism**
  - **Bioterrorism has generally involved a limited range of agents**
  - **Limited dissemination capabilities**
  - **Limited potential to cause a high consequence BW event**
  - **Intent and effect of BW use has been primarily tactical, but potentially strategic in the future**

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Acquisition for Biological Weapons

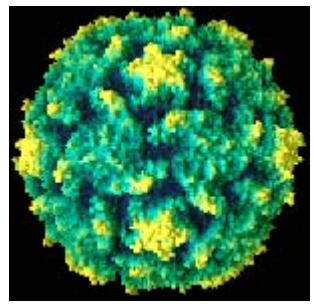
- Sources of *high risk agents*
  - Natural environment
    - Natural reservoirs
    - Disease outbreaks
  - Legitimate facilities
    - Bioscience facilities
    - Culture collections
    - Clinical facilities
  - Synthetic biology
    - De-novo synthesis
    - Genetic modifications
    - Drug resistance

- Technical requirements
  - Identify and isolate material
  - Select strain

De-novo Synthesis of Biological Weapons

- **Published experiments**
  - 2002 – polio virus
  - 2003 – phi-X174 virus
  - 2005 – 1918 Spanish Influenza pandemic virus
- **Materials**
  - DNA synthesizer
  - DNA sequencer
  - Nucleotides, plasmids, enzymes
- **Challenges**
  - Obtaining complete, accurate genome
  - Correct synthesis of large genomes
  - Avoiding minor errors resulting in loss of desirable attribute (e.g. virulence, hardiness, transmissibility…)
  - Outsourcing of DNA sequencing may attract attention
- **Challenges are diminishing with time**
  - More genomes being sequenced, improved accuracy
  - Improved techniques
  - Protocol refined through documented research, experienced scientists

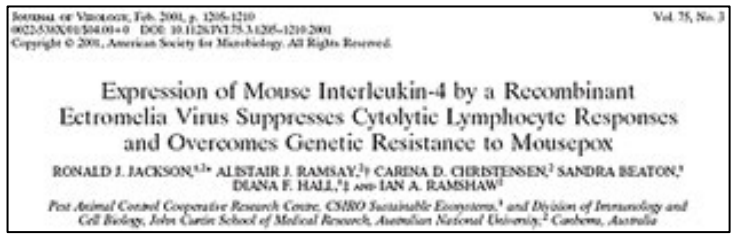
DNA Synthesizer



Polio Virus

Genetic Modification for Biological Weapons

- **Published experiments**
  - **2001 – IL-4 mousepox**
- **Materials**
  - **DNA splicer**
  - **Plasmids**
- **Challenges**
  - **Identification of correct strand to modify; knowledge of how to modify it**
  - **Need to avoid unintended effects that weaken desirable attributes**
  - **Difficult to predict which modifications will create desired effect**
- **Technical hurdles diminishing with time**
  - **Expertise in genetic engineering growing rapidly with the advance of biotechnology**
  - **Further availability of relevant technologies and equipment**



JOURNAL OF VIROLOGY, Feb. 2001, p. 1205–1210 Vol. 75, No. 3
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Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox

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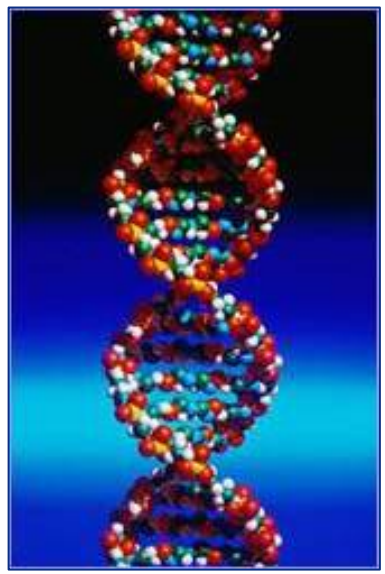

Production of Biological Weapons

- **Goal: adequate quantity in an adequate form**

- **Technical requirements**
  - **Amplification**
    - **Appropriate growth media**
    - **Rapid PCR**
  - **Processing**
    - **To withstand environmental stressors**
    - **To survive dissemination**
    - **To aerosolize for optimal dissemination**
  - **Storage**

Dissemination of Biological Weapons

- **Primary modes of concern**
  - **Inhalation**
  - **Oral**
- **Technical requirements**
  - **Development of effective delivery mechanism**
  - **Assessment of meteorological conditions**

Technological Advances can Lower the Barrier for Bioterrorism

- **Acquisition**
  - **Publications, patents, internet-based outbreak monitoring provide increasing information on the location of high risk agents**
  - **Technology, tools, and skills to create high-risk agents are becoming more widespread**
- **Production**
  - **Internet is a ready source for instructions on amplifying and processing**
  - **Kits**
- **Dissemination**
  - **Rapid global travel and economic ties can make consequences more significant**
  - **Pharmaceutical and agricultural companies are developing efficient aerosol delivery systems**

The "Dual – Use" Dilemma

Scenarios for State Biological Weapons Proliferation

Objectives	Acquisition	Development	Dissemination
• Defensive use in asymmetric scenario • Offensive use in regional conflicts between symmetric states • Battlefield or other territory denial • Troop incapacitation	• Legitimate lab or culture collection (theft or fraud) • Provided by another State • Derived from natural sources • Genetic engineering or chemical synthesis • Theft from transport	• Advanced laboratory capabilities - Weaponize - Grow - Test - QA - Store - Transport	Sophisticated dissemination methods: • Ordinance (battlefield) • Missile • Airplane / UAV • Large-scale sprayer

Scenarios for Non-State Biological Weapons Proliferation

Objectives	Acquisition	Development	Dissemination
•Generate terror •Promote geopolitical objectives •Genocide •Invigorate support base •Assassination	•Legitimate lab or culture collection (theft or fraud) •Theft from transport •Derived from natural sources •Provided by hostile state actor	•Tactical quantities •Limited development / weaponization •Use proven bugs (non GMOs for at least the next 5 years)	•Natural (human vector) •Commercial sprayers •Unconventional - mail systems •Food / water •Building HVAC systems •Percutaneous inoculation

"A Biological Weapons Risk Assessment"

Scenario	Probability	Consequences	Risk
Biocrimes	High based on historical evidence	Very low by definition	Low
Biological warfare (non-rogues states)	Very low based on historical record	High based on technical sophistication of non-rogue states	Low
Biological warfare (rogue states)	Low based on historical record	Moderate based on technical sophistication of rogue states	Low to moderate
Bioterrorism (non-state actors)	Low to moderate based on historical evidence, but increasing	Low to moderate based on the historical record and technical expertise, but increasing	Low to moderate, **BUT Increasing**

Salerno et al., *Nonproliferation Review* (Fall-Winter 2004)

Evolution of the Biological Weapons Threat

- Experts generally agree that the biological weapons are more likely to be sought after and used by terrorists than states
- Technologies and expertise required to produce and deploy biological weapons are widely available and dual use
  - Future advances in biotechnology will make the menace of biological weapons increasingly accessible and attractive to terrorists
- Limiting step for most bioterrorists is acquiring the viable and virulent pathogen
  - Source materials are widely available in legitimate bioscience facilities internationally
- Protecting legitimate bioscience globally is a critical prevention measure to reduce the bioterrorist threat

Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus

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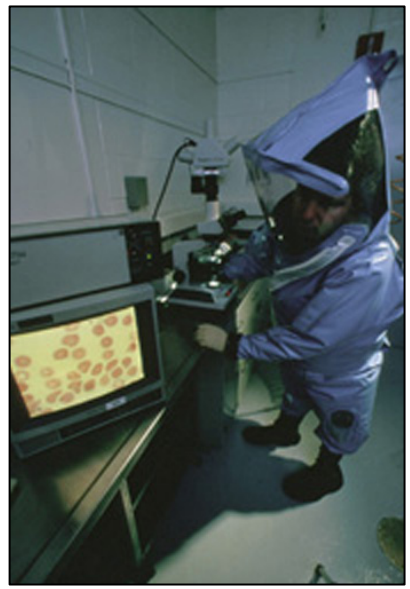
Challenges for the Development of Preventive Solutions

- Terrorists no longer need sophisticated processing and dissemination systems to threaten international security
- Materials, technologies, and expertise are distributed among thousands of legitimate bioscience facilities worldwide
- Excessive controls on the biotechnology industry will jeopardize critical research without providing tangible security benefits



"I would say that acquiring [CBRN] weapons for the defense of Muslims is a religious duty."
Bin Laden to Rahimullah Yusufazi, 1998

Conclusions

- The threat of bioterrorism has become the principal component of the overall BW threat
- This change has been driven primarily by the expansion of “dual-use” biotechnology
  - Continues to broaden the base of materials, technologies, and expertise needed to produce a weapon
- Imperative to devise solutions that promote the continuation of beneficent bioscience, while also reducing the likelihood that it can be misused
- Laboratories have a responsibility to work safely and securely with dangerous pathogens
- International collaboration is critical to mitigate the BW threat